REMARKS

The Office Action dated March 17, 2020 has been carefully considered and the following response prepared. Claims 1-7, 9, 15 and 16 are pending in the application.

Rejections under 35 USC 112, First Paragraph, Written Description and Enablement, and Objection to the Specification under 35 USC 132, New Matter

At pages 2-5 of the Office Action, the Examiner maintained the rejections under 35 USC 12, first paragraph, as not enabled and failing to comply with the written description requirement, but did not specify the claims to which the rejections applied. At page 4 of the Office Action, the Examiner rejected claims 1-7 and 9 under 35 USC 112, first paragraph, as failing to comply with the written description requirement. At pages 4-5 of the Office Action, the Examiner objected to the specification under 35 USC 132, alleging that the specification contains new matter. The grounds for each of the rejections, and the objection to the specification relate to amendments to the claims and specification made in the Submission filed March 1, 2010. The Examiner contended that the schemes, diagrams and description in the specification do not match the claims or the amended variables.

Applicants traverse the foregoing rejections of the claims and objection to the specification. Applicants filed a Supplemental Submission on March 11, 2010 that contains amendments to the diagrams and schemes, as explained in the Supplemental Submission, so that the variables in the specification, diagrams, and claims are consistent. Applicants incorporate by reference herein the Supplemental Submission, and request consideration by the Examiner in conjunction with the present response. When the amendments in the Supplemental Submission are considered with the amendments in the Submission, the Examiner will find that the schemes, diagrams and description in the specification match the claims and amended variables, and overcome the specific grounds for each rejection and the objection to the specification. No new matter has been added by the Submission filed March 1, 2010 or the Supplemental Submission filed March 11, 2010.

In view of the foregoing, Applicants have overcome the rejections under 35 USC 112, first paragraph, and the new matter objection under 35 USC 132. Withdrawal of the rejections and objections to the specification are respectfully requested.

Rejection under 35 USC 103

At page 4 of the Office Action, the Examiner maintained the rejection of claims 1-7, 9, 15 and 16 under 35 USC 103 as being *prima facie* obvious over U.S. patents 4,584,377 (Yokoi et al.); 4,673,678 (Misra) and 5,166,208 (Kelly et al.). Duan et al., Delgado et al. and Okimoto et al. were also used to reject the claims.

Applicants again traverse this rejection.

In the Office Action mailed October 1, 2009, the Examiner alleged that the claims still have numerous generic definitions, and that glucose, fructose, other hetero groups, and cyclodextrin can all be encompassed by them. In the present Office Action, the Examiner alleged that Applicants have not amended the claims to overcome the rejection of the claims as obvious.

Claims 1-7 are directed to compounds of Formula Ia and Formula Ib, as set out in the claims. The compounds of claims 1-7 are fredericamycin derivatives. Claim 9 is directed to drugs containing compounds according to claim 1, a carrier and adjuvants. Claims 15 and 16 are directed to methods of treating tumors and parasites, respectively, by administering a compound according to claim 1.

Claim 1 was previously amended to delete reference to sugars in substituents R5, R21 and R22. The compounds of Formula Ia and Formula Ib in claims 1-7 are defined so that the claimed compounds do not overlap with the compounds disclosed in Yokoi et al, Misra and Kelly et al.; see in particular the definitions of R2 and R3. In the Supplemental Submission submitted March 11, 2010, which is incorporated by reference herein, the specification was amended to correct an obvious error in the English translation of the definition of "cycloalkyl" at page 12, in the last paragraph. The definition of "cycloalkyl" was amended to state that cycloalkyl "comprises unsaturated (mono or poly, preferably mono) or saturated, cyclic hydrocarbon groups with 3 to 10 C atoms."

In the present Office Action, the Examiner's comments to this rejection appear to acknowledge that Yokio et al., Misra and Kelly et al do not disclose the claimed compounds. The Examiner is respectfully requested to point out the specific parts of the claims that can encompass glucose, fructose, other hetero groups and cyclodextrins in the next Office Action, if this rejection is not withdrawn.

A *prima facie* case of obviousness requires the following: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference (or references when combined) must teach or suggest all the claim limitations. MPEP at 2143.

The Examiner bears the initial burden of establishing *prima facie* obviousness. *See In re Rijckaert*, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). To support a *prima facie* conclusion of obviousness, the prior art must disclose or suggest all the limitations of the claimed invention. *See In re Lowry*, 32 F.3d 1579, 1582 (Fed. Cir. 1994); *see also Abbott Labs. v. Sandoz, Inc.*, 544 F.3d 1341 (Fed. Cir. 2008) ("[t]he KSR opinion ... did not mention or affect the requirement that each and every claim limitation be found present in the combination of the prior art references before the analysis proceeds.").

The Examiner has not met the initial burden of establishing *prima facie* obviousness. The three cited patents Yokoi et al, Misra and Kelly et a. each disclose fredericamycin A derivatives, but do not disclose or suggest the compounds of claim 1-7. Duan et al., Delgado et al. and Okimoto et al. disclose cyclodextrin for use in inclusion complexes with drugs that are poorly water soluble. However, there is no disclosure or suggestion that the cyclodextrin complexes can be used with fredericamycin A derivatives.

Even if, for the sake of argument, the teachings of the references were properly combined, the combined teaching of the cited references would still not disclose the compounds of claims 1-7, the drugs of claims 9-10 that contain the compounds of claim 1, or the methods of claims 15 and 16 which employ the compounds of claim 1. At most, the combined teachings of the cited references would provide cyclodextrin inclusion complexes containing <u>different</u> fredericamycin derivatives than the claimed compounds. Thus, even if combined, the combined

teaching of the cited references does not teach or suggest every limitation of the claims and accordingly, a *prima facie* case of obviousness has not been established. For this reason alone, the rejection should be withdrawn.

In the present Office Action, the Examiner commented that she made an obviousness rejection with showing of motivation and reason to combine it with fredericamycin (a drug see claim 9), and that the exact same drug does not have to be taught. The Examiner contended that there is sufficient reason and motivation to combine the references and so the rejection has been maintained.

Applicants respectfully disagree. Applicants submit that the motivation and reasons provided by the Examiner for combining the references are not sufficient to establish a *prima facie* case of obviousness. To establish a *prima facie* case of obviousness, the same compounds must be taught or suggested by the combination of references. The combination of Yokoi et al., Misra, Kelly et al., Duan et al., Delgado et al. and Okimoto et al. does not teach or suggest the compounds of claims 1-7, the drugs of claim 9, or the methods of claim 15 and 16.

Moreover, the Examiner's stated motivation and reasons for combining the references does not address claims 1-7, which are directed to compounds of Formula Ia and Ib, as defined in the claims, not pharmaceutical compositions, or drugs as the pharmaceutical compositions are referred to in claim 9. [R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness.'" *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398, at ___, 82 USPQ2d 1385, at 1396 quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). The Examiner has provided no motivation or pointed to anything in the cited references or knowledge in the art that would lead a person skilled in the art to modify the teachings of Yokoi et al., Misra or Kelly et al., or the other cited references, Duan et al., Delgado et al. and Okimoto et al., to obtain the compounds of claims 1-7. The combined teachings of the cited references are likewise insufficient to render obvious the drugs of claim 9 which contain the compounds of claim 1, and the methods of claims 15 and 16 which employ the compounds of claim 1, for the same reasons.

The rejection of claims 1-7, 9, 15, and 16 is improper and should be withdrawn. For at

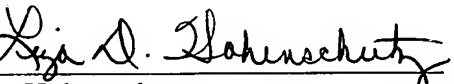
least the reasons discussed above, the rejection of claim 1-7, 9, 15, and 16 is deficient, and does not establish a *prima facie* case of obviousness. The Examiner has provided no motivation or reason to modify the teachings of the cited references to obtain the compounds of claims 1-7. The combined teachings of the cited references do not disclose or suggest all of the limitations of the compounds of claims 1-7, the drugs of claim 9 which contain the compounds of claim 1, and the methods of claims 15 and 16 which employ the compounds of claim 1. Claims 1-7, 9, 15, and 16 are not *prima facie* obvious in view of the combined teachings of Yokoi et al., Misra, Kelly et al., Duan et al., Delgado et al. and Okimoto et al. Withdrawal of this section 103 rejection is again respectfully requested.

In view of the above, the present application is believed to be in a condition ready for allowance. Reconsideration of the application is respectfully requested and an early Notice of Allowance is earnestly solicited.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 03-2775, under Order No. 14528-00001-US from which the undersigned is authorized to draw.

Dated: June 17, 2010

Respectfully submitted,

By 

Liza D. Hohenschutz
Registration No.: 33,712
CONNOLLY BOVE LODGE & HUTZ LLP
1007 North Orange Street
P. O. Box 2207
Wilmington, Delaware 19899-2207
(302) 658-9141
(302) 658-5614 (Fax)
Attorney for Applicant